Hemoglobin A1C (A1C)

- A1C target goals have been lowered. The ADA suggests a target A1C < 7 percent. The American College of Endocrinology supports a target A1C < 6.5 percent.
- The ADA recommends re-evaluation and significant change in treatment for anyone with an A1C > 8 percent.
- Perform A1C testing at least two times a year in patients who are meeting treatment goals and who have stable glycemic control.
- Perform A1C testing quarterly in patients whose therapy has changed or who are not meeting glycemic goals.
- Use of point-of-care testing for A1C allows for timely decision-making regarding therapy changes, when indicated.
- Glycemic control is best determined by evaluating a combination of both the patient's SMBG results and A1C results.
- In 2006, 91.6 percent of BRFSS respondents with diabetes stated a healthcare professional had checked their A1C at least once in the previous year.
- The *Healthy People 2010 Objective 5-12* is to increase the proportion of adults with diabetes who have an A1C measurement at least once a year.

What is A1C?

A1C is one of a group of stable minor hemoglobin components, glycated hemoglobin, formed slowly and nonenzymatically from hemoglobin and glucose. The rate of formation of A1C is directly proportional to the level of blood glucose. A single sample of hemoglobin contains red cells of various ages. Since the average life of a red cell is four months, a single A1C level reflects the blood sugar levels that red cells have been exposed to in the previous two to three months. Thus, A1C levels reflect the average of a person's blood sugar levels in the past two to three months. Certain clinical situations, including frequent episodes of hypoglycemia, may alter the A1C level. Any clinical situation that increases erythrocyte turnover and increases the percentage of young circulating erythrocytes, such as a hemolytic anemia, will lower the measured A1C level. Other clinical situations may interfere with the assay methodology, e.g. hemoglobinopathies, chronic alcohol ingestion, salicylates, uremia, and sample storage effects.

How often should an A1C be obtained?

The A1C level should be measured at least every six months in all persons with diabetes. More frequent monitoring is appropriate if a person's diabetes is not in control or if there are significant changes in management. A1C testing should be dependent on the clinical situation, the treatment regime used, and the judgment of the clinician (ADA, 2007).

What assay does my lab use?

There are several different types of assays for glycated hemoglobin. Some assays measure A1C directly; others actually measure total glycated hemoglobin and derive a calculated A1C result. The range of normal varies between assay types. Clinicians should be aware of the specific assay used in their laboratory and the range of normal values. If a patient changes the laboratory that measures their A1C, the clinician should consider that the results may vary from previous results because of a change in methodology and/or a new range of normal and not because of a change in the patient's clinical status.

What is the goal for A1C?

The American Diabetes Association (ADA) recommends a goal A1C of < 7 percent. Practitioners should re-evaluate, and in most cases significantly change, the treatment regime for anyone with A1C levels consistently > 8 percent. The American College of Endocrinology (ACE) and the American Association of Diabetes Educators (AADE) are recommending a target A1C of 6.5 percent. This more rigorous target goal is consistent with goals currently in place in Europe. In patients without diabetes, an A1C of 4 to 6 percent is considered normal.

Glycemic control markedly reduces the progression of microvascular complications. In the type 1 patients followed in the landmark Diabetes Control and Complications Trial, there was a 45 percent lower rate of progressive retinopathy in persons with a mean A1C of 8.2 percent as compared to patients with a mean A1C of 9 percent. Patients with a mean A1C of 7.2 percent had a rate of progressive retinopathy 33 percent lower than patients with a mean A1C of 8 percent. Glycemic control also delayed the onset and progression of renal disease and diabetic neuropathy. More recent clinical trials continue to defend conclusions that improved glycemic control reduces risk of developing retinopathy and reduces cardiovascular disease events.

Individualized goal setting to attain a hemoglobin A1C level less than 7 percent is recommended in the majority of patients. However, less stringent treatment goals may be appropriate for patients who are frail, elderly, experience adverse effects related to tight control, and those who have a short life expectancy due to comorbid conditions.

Tight glycemic control benefits type 2 patients as well. The initial results of a major study of the effect of tight glycemic control in type 2 patients, the United Kingdom Prospective Diabetes Study (UKPDS), were published in 1998. The principal conclusions of that study to date are:

- Vigorous treatment of hyperglycemia decreases the morbidity and mortality of type 2 diabetes.
- Glycemic control reduces the risk of developing retinopathy, neuropathy, and nephropathy. The overall rate of microvascular complications was 25 percent lower in the intensive therapy group than in the conventionally treated group.
- The use of insulin, sulfonylureas, and metformin does not increase the risk of cardiovascular complications, thus there are no reasons not to treat glycemic levels aggressively.
- Control of blood pressure reduces the risk of both microvascular and macrovascular disease.
- The effects of glycemic control and blood pressure control are additive.
- The effect of tight glycemic control on reducing the risk of major cardiovascular events (myocardial infarction, stroke, amputation, and sudden death) did not reach statistical significance, though patients with the highest levels of glycemia experienced a greater incidence in major events.

What is the newest consensus statement of A1C measurement?

The American Diabetes Association, European Association for the Study of Diabetes, International Federation of Clinical Chemistry and Laboratory Medicine, and the International Diabetes Federation are calling for universal, worldwide standardization values for measurement of hemoglobin A1C. They have released a new equation and a new system for reporting blood glucose results. The new number will be reported as ADAG (A1C derived average glucose).

Knowledge gained from the American Association of Diabetes Glucose Trials (ADAG) indicated that elevated A1C values increase the chances of microvascular complications from diabetes. Clinicians worldwide are calling for a universal measurement to monitor glycated hemoglobin A1C levels, with reporting of test results in scientifically correct units such as mmol/L, as a percentage value is not a measure. Results from the American Association of Diabetes Glucose Trials (ADAG) have identified a new equation to make numerical assessments of glycemic control more accessible to patients. Refer to the website for additional information www.easd.org.

The equation: AG (average glucose in mmol/L) = 1.583 x HbA1C – 2.52. Where R2* = 0.836 mmol/L. (Note that 1 mmol/L = 18mg/dl.) With this system, providers will have three numbers: the usual A1C percentage, the new IFCC version in mmol/L, and the new estimated average glucose.

**R2 is defined as the root mean square error (the standard deviation of prediction error).*

The implications are that patients will find it easier to integrate this information into their management behaviors and improve control because the average glucose scale matches that of glucose meters. Also, manufacturers of A1C equipment will need to update their software. Prior to this new information, the A1C was tied to the results of the DCCT, where a 6 percent was equal to 135 mg/dL. The change occurred as a result of checking and comparing values between A1Cs and values from over two thousand finger sticks and averaging them out. Thanks in part to new technology, data from thousands of finger sticks, and use of continuous blood glucose monitors, results are more accurate. Use of this equation yields a linear correlation with a wide range of A1C values. This means that a 6 percent A1C reading in no longer an average of 135 mg/d. The new number values are as follows:

- 6% = 126mg/dl
- 7% = 155 mg/dl
- 8% = 182 mg/dl
- 9% = 211 mg/dl
- 10% = 239 mg/dl

Which measure is more important, the A1C or blood glucose? The ADAG trial showed no difference between LifeScan Monitor and CGM data. Conclusions from the study show that perhaps A1C is not the gold standard for correlating cardiovascular disease with glucose levels. Data presented at EASD showed that patients with the same A1C can have different “area under the curve” postprandial glucose (PPG). For these patients, high PPG values may be a better indicator of inflammation and CVD risk than A1C. It should be the combinations of data that will most help patients understand how the A1C and the average blood glucose are both important. (Reported at 2007 EASD Symposium)

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